

Preconception care for women with type 1 diabetes

Jennifer A. Klinker, MD Ellen L. Toth, MD, FRCPC

ABSTRACT

OBJECTIVE To emphasize preconception care of women with type 1 diabetes and the role of primary care physicians in evaluating and counseling them.

QUALITY OF EVIDENCE Substantial level II evidence indicates that tight glycemic control before conception and early in pregnancy reduces the rate of congenital malformations. Most evidence concerning maternal and fetal risks during pregnancy in patients with type 1 diabetes is level III or IV. Little is published on the role of family physicians in providing preconception counseling or care.

MAIN MESSAGE Preconception care is effective in improving glycemic control early in pregnancy and in reducing the rate of congenital malformations. Preconception evaluation of type 1 diabetic patients involves assessment of prepregnancy glycemic control and diabetic complications. Preconception counseling includes discussing the rate of transmission of diabetes, the effects of pregnancy on maternal and fetal complications, and the use of contraception until optimal glycemic control can be attained.

CONCLUSION Primary care physicians often have frequent and early contact with women of reproductive age; they are ideal candidates for providing type 1 diabetic women with preconception evaluation and counseling.

RÉSUMÉ

OBJECTIF Faire le point sur la prise en charge des femmes avec un diabète de type 1 avant la conception et sur le rôle du médecin de première ligne pour évaluer ces patientes et les conseiller.

QUALITÉ DES PREUVES Des preuves convaincantes de niveau II indiquent qu'un contrôle serré des glycémies avant la conception et en début de grossesse réduit le taux de malformations congénitales. Les preuves concernant les risques maternels et fœtaux de la grossesse chez les patientes souffrant de diabète de type 1 sont pour la plupart de niveaux III et IV. Très peu d'articles traitent du rôle du médecin de famille comme source de conseils et de soins avant la conception.

PRINCIPAL MESSAGE La prise en charge des patientes avant la conception est efficace pour améliorer le contrôle de la glycémie en début de grossesse et réduire le taux de malformations congénitales. Avant la conception, l'évaluation des patientes souffrant de diabète de type 1 porte, entre autres, sur le contrôle de la glycémie et les complications diabétiques pré-existantes. Les discussions à cette étape portent sur le taux de transmission du diabète, sur les complications maternelles et fœtales pouvant résulter de la grossesse et sur l'utilisation de contraception jusqu'à ce qu'un contrôle optimal de la glycémie soit atteint.

CONCLUSION Plusieurs médecins de première ligne ont des contacts fréquents et précoces avec des femmes en âge de concevoir; ils sont donc très bien placés pour évaluer et conseiller les femmes souffrant de diabète de type 1 avant la conception.

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Cet article a fait l'objet d'une évaluation externe.

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An estimated two million Canadians have diabetes mellitus: 10% of them have type 1 diabetes. Given the usual early onset of type 1 diabetes, most of these patients will have diabetes during their peak reproductive years.

Organogenesis occurs within the first 8 weeks of gestation, before most women know they are pregnant. It has been well documented that elevated HbA_{1c} levels in early pregnancy are associated with increased risk of congenital anomalies and spontaneous abortions.^{1,3} The rate of congenital anomalies among offspring of women with type 1 diabetes approaches that among offspring of nondiabetic women when strict glycemic control is achieved before conception.⁴ Thus, it is essential that all diabetic women of childbearing age be educated about the importance of tight glycemic control before conceiving.

Given the nature of general practice, family practitioners often have frequent and early contact with women of childbearing age. Primary care physicians, therefore, are in an ideal position for providing preconception care. This update outlines essential elements family physicians should include when evaluating and counseling patients with type 1 diabetes before they conceive.

Quality of evidence

MEDLINE, EMBASE, CINAHL, Web of Science, and Cochrane databases were searched using the key words "diabetes mellitus, insulin-dependent"; "pregnancy in diabetes"; "preconception care"; "prepregnancy care"; "physicians, family"; and "counseling." The search was limited to English-language articles. Because type 1 diabetes is a relatively new term, insulin-dependent diabetes was the main search term used to maximize results. References from all studies were searched for further relevant publications.

Articles were selected based on the best available evidence concerning both pregnancy-associated risks in type 1 diabetes and preconception evaluation and counseling. Levels of evidence ranged from II to IV. Most studies were small prospective or retrospective studies. We were unable to find any current relevant publications on family physicians' role

Dr Klinke is a third-year Internal Medicine Resident in the Department of Medicine at the University of Alberta in Edmonton. **Dr Toth** is a Professor in the Division of Endocrinology and Metabolism in the Department of Medicine, is a Fellow of the Institute of Health Economics at the University of Alberta, and is a diabetes specialist on staff at the University of Alberta Hospitals.

in providing preconception counseling and care to type 1 diabetic patients.

Preconception care

Preconception care includes evaluating both diabetes control and complications and counseling on the risks of pregnancy. According to Canadian Diabetes Association clinical practice guidelines, any woman with diabetes planning a pregnancy should be assessed for level of glycemic control and status of any diabetic complications.⁵ Preconception evaluation should consist of a thorough history and physical examination in conjunction with laboratory investigations. Specifically, any history of gastroparesis, hypoglycemic unawareness, or orthostatic hypotension should be sought, as these conditions can compromise maternal health during pregnancy.

Hemoglobin (HbA_{1c}) should be measured. Creatinine clearance and 24-hour microalbumin excretion tests are required before conception and at regular intervals during pregnancy. Thyroid function tests are also indicated, as 5% to 10% of patients with type 1 diabetes have concomitant thyroid disease.⁶ Referral to an ophthalmologist for evaluation of any pre-existing retinopathy should be made.⁵ Finally, a prepregnancy exercise stress test should be considered for those with increased cardiac risk (ie, diabetes duration longer than 20 years, hyperlipidemia, signs or symptoms of vascular disease). A stress test could also be considered for those with cardiovascular autonomic neuropathy, as symptoms of myocardial infarction can be masked.⁷ **Table 1** summarizes the preconception workup.

Preconception counseling should involve discussion of the risk of transmitting diabetes, the risk of congenital anomalies, fetal and maternal complications of pregnancy, and the need for pregnancy planning^{6,8} (**Table 2**).

Risk of transmitting diabetes to offspring

Patients can overestimate their chances of transmitting type 1 diabetes to their children. One large prospective trial in Finland, which has the world's highest incidence of type 1 diabetes, looked at the risk of developing diabetes in 9453 offspring of type 1 diabetic parents. The cumulative risk of developing diabetes by age 20 was 5.3%. Further, there was a sex-specific difference: offspring of diabetic fathers had a cumulative risk of 7.6%; offspring of diabetic mothers had a risk of 3.5%.⁹ Thus, men with type 1 diabetes have a greater chance of passing the disease on to

Table 1. Prepregnancy workup of women with type 1 diabetes

Thorough history and physical examination
Hemoglobin (HbA _{1c}) assessment
Creatinine clearance* and 24-hour microalbumin tests
Thyrotropin measurement
Ophthalmology referral
Possibly exercise stress test

**Creatinine clearance is a more accurate assessment of baseline renal function than measurement of serum creatinine alone. Normally, creatinine clearance increases during pregnancy as the glomerular filtration rate increases.*

Table 2. Key issues to be discussed during preconception counseling

The risk of transmitting type 1 diabetes is 3.5% to 7.6%.

Poor glycemic control before and during early pregnancy is associated with an increased risk of spontaneous abortions and congenital malformations.

Both retinopathy and nephropathy can progress during pregnancy; autonomic neuropathies can complicate a pregnancy.

Pregnancies must be planned. Contraception should be used until optimal glycemic control is achieved.

their children. Overall, however, the transmission rate of type 1 diabetes is quite low.

Risk of neonatal morbidity and mortality

Poor glycemic control during the first trimester is associated with increased risk of spontaneous abortion and congenital malformations.⁴ Major congenital malformations associated with diabetes involve abnormalities of the skeletal, gastrointestinal, genitourinary, cardiac, and central nervous systems.¹⁰ Preconception HbA_{1c} less than 3.5 standard deviations above the normal mean is believed to be ideal⁷ (eg, the HbA_{1c} should be less than 6.8% for laboratories where the upper limit of normal is 6.1%). At such a level, the rate of congenital anomalies is similar to that of nondiabetic mothers. Target glucose levels in preparation for conception and during pregnancy are fasting <5.3 mmol/L, and 2-hour postprandial <6.7 mmol/L.⁵

Other pregnancy risks in type 1 diabetes include macrosomia and neonatal hypoglycemia. As well, intrauterine growth retardation, preeclampsia, and preterm delivery can complicate pregnancies in the presence of maternal nephropathy.¹¹ Neonatal morbidity associated with smoking, alcohol use, and folate deficiency are concerns—just as they would be in nondiabetic pregnancies.

Risk of maternal complications

Women with type 1 diabetes need to be educated about the effect of pregnancy on complications of their diabetes. Retinopathy can progress during pregnancy.¹² Worsening of retinopathy is correlated with higher HbA_{1c} levels and possibly with rapid improvement of metabolic control.¹⁰⁻¹³ In order to document baseline status, patients should be seen by an ophthalmologist before conceiving. If no abnormalities are present initially, patients can generally be reassured. Women with background retinopathy should anticipate repeated ophthalmologic examination during pregnancy. If any proliferative changes are found, they are best treated before pregnancy.⁷

Development and progression of diabetic nephropathy during pregnancy is associated with poor blood pressure and glycemic control.¹¹ Progression of diabetic nephropathy also depends on baseline renal function before conception. If baseline renal function is normal, mild proteinuria can develop during pregnancy, but it resolves postpartum. One third of cases where baseline microalbuminuria exists will progress to nephrotic-range proteinuria by the end of the pregnancy. Finally, most women who have preconception macroproteinuria (>200 mg/d) will become nephrotic and are at higher risk of developing proliferative retinopathy and preeclampsia.⁷ Women who have very poor renal function (creatinine clearance <50 mL/min) should be advised to avoid pregnancy, but could reconsider it after successful renal transplantation.¹⁰ It is important to note that angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers should be discontinued before conception, as they have been shown to be fetopathic (eg, intrauterine growth retardation, pulmonary hypoplasia, oligohydramnios).¹⁴

Autonomic neuropathies, such as gastroparesis, diabeticorum, urinary retention, hypoglycemic unawareness, and orthostatic hypotension, are important to identify before conception, as these conditions can complicate pregnancy. If patients have morning sickness, gastroparesis can result in labile glucose levels and decreased oral intake. If patients are unaware they have hypoglycemia, target glucose levels might have to be more liberal to avoid hypoglycemic reactions.⁷ Peripheral neuropathy can be exacerbated by pregnancy, especially compartment syndromes (such as carpal tunnel syndrome).⁶

Hypertension should be treated to maintain systolic blood pressure below 130 mm Hg and diastolic blood pressure below 85 mm Hg. Antihypertensive agents safe for pregnancy include methyldopa, clonidine,

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and β -blockers (other than atenolol, which has been associated with infants small for gestational age). Hydralazine and labetalol can be used for treating acute severe hypertension.¹⁴

Pregnancy planning

Given the consequences of poor glycemic control early in pregnancy, diabetic women of childbearing age should plan their pregnancies. Pregnancy planning implies using contraception until circumstances are ideal to pursue pregnancy. Those thinking of conceiving need to be warned that it can take months of intense effort to adjust diet, exercise, and insulin dosage, in order to obtain ideal metabolic control. Even for those already receiving intensified treatment, further lifestyle changes will be required. Patients could be asked to perform home blood glucose monitoring more frequently throughout the day. Visits to a diabetologist will likely be required.

The choice of contraception while awaiting ideal metabolic control depends mostly on the couple's preference. Prospective studies evaluating the use of low-dose combination or progestin-only pills among women with type 1 diabetes have shown these medications to have minimal effect on glycemic control.^{8,10}

Preconception clinics

Many studies have looked at the efficacy of structured preconception clinics for women with diabetes. These focused programs are successful in obtaining good glycemic control early in pregnancy and in reducing perinatal mortality and malformation rates.^{15,16} There is also some evidence that preconception diabetes care can reduce neonatal morbidity, suggested by a reduction in the rate of macrosomia and the rate of admission to neonatal care units.¹⁷ Women more likely to plan their pregnancies and seek preconception care are married, are employed, and have higher levels of education and income.¹⁸⁻²⁰ They often have positive relationships with their health care providers. These women indicate having had reassuring and encouraging advice from their physicians before pregnancy.¹⁹

Despite the evidence that preconception clinics are effective, they are not always available because of geographic location or health care system limitations. Ideally, family physicians should be able to refer type 1 diabetes patients for the detailed assessment and intensive management they require. Given the nature of their practice, however, family doctors have an early opportunity to initiate preconception discussions with all their type 1 diabetic patients of

Editor's key points

- Ten percent of diabetic patients in Canada are type 1, and most of them will have diabetes during their reproductive years.
- Good evidence shows that poor glycemic control early in pregnancy increases the risk of congenital abnormalities and spontaneous abortions.
- Strict control of diabetes reduces these risks to levels similar to those of nondiabetic women.
- Preconception workup includes HbA_{1c}, creatinine clearance, 24-hour urine assessment for microalbuminuria, thyroid function, ophthalmology referral, and possibly a stress test. Counseling should address preconception contraception, maternal and fetal complications, and the risks of transmitting diabetes to offspring.
- Maternal complications of pregnancy with diabetes include worsening or development of retinopathy, nephropathy, and autonomic neuropathy.
- Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers should be discontinued before pregnancy due to fetal complications.


Points de repère du rédacteur

- Au Canada, 10% des diabétiques sont du type 1 et la plupart souffriront de diabète durant leurs années de reproduction.
- Il est bien démontré qu'un mauvais contrôle des glycémies en début de grossesse augmente le risque d'anomalies congénitales et d'avortements spontanés.
- Un contrôle strict du diabète ramène ces risques aux mêmes niveaux que ceux des femmes non diabétiques.
- L'évaluation avant la conception comprend la mesure de l'HbA_{1c}, de la clairance de la créatinine, de la microalbuminurie des 24 heures et de la fonction thyroïdienne, une consultation en ophtalmologie et parfois une épreuve d'effort. Les conseils devraient porter sur la contraception avant la conception, les complications maternelles et fœtales, et le risque de transmission du diabète à l'enfant.
- Les complications maternelles de la grossesse chez une diabétique incluent l'apparition ou l'aggravation d'une rétinopathie, d'une néphropathie ou d'une neuropathie neuro-végétative.
- Les inhibiteurs de l'enzyme de conversion de l'angiotensine et les bloqueurs des récepteurs angiotensine devraient être cessés avant la grossesse en raison de complications fœtales.

reproductive age. It cannot be stressed enough how important it is to initiate these discussions early on,

no matter how apparently remote the chances of the patient's conceiving appear. Every visit with a diabetic woman can be regarded as a preconception visit.

Conclusion

Family physicians have an important role in the preconception care of patients with type 1 diabetes. Preconception evaluation should include a thorough history, physical examination, and laboratory tests to assess maternal and fetal risks of pregnancy. Counseling should involve discussions of the rate of transmission of diabetes, the effects of pregnancy on maternal and fetal complications, and the role of contraception while awaiting successful control of glycemia. Finally, women with diabetes should be reassured that a planned pregnancy with adequate glycemic control before conception and early during gestation increases the likelihood of a good outcome: a healthy baby and mother. 

Competing interests

None declared

Correspondence to: Ellen L. Toth, MD, 362 HMRC, Department of Medicine, University of Alberta, Edmonton, AB T6G 2S2; telephone (780) 407-6223; fax (780) 407-6702; e-mail ellen.toth@ualberta.ca

References

1. Suhonen L, Hiilesmaa V, Teramo K. Glycaemic control during early pregnancy and fetal malformations in women with type 1 diabetes mellitus. *Diabetologia* 2000;43:79-82.

2. Kitzmiller JL, Gavin LA, Gin GD, Jovanovic-Peterson L, Main EK, Zigrang WD, et al. Preconception care of diabetes: glycemic control prevents congenital anomalies. *JAMA* 1991;265:731-6.
3. Jovanovic L, Druzin M, Peterson CM. Effect of euglycemia on the outcome of pregnancy in insulin-dependent diabetic women compared with normal control subjects. *Am J Med* 1981;71:921-61.
4. Greene MF. Spontaneous abortions and major malformations in women with diabetes mellitus. *Semin Reprod Endocrinol* 1999;17:127-36.
5. Meltzer S, Leiter L, Daneman D, Gerstein HC, Lau D, Ludwig S, et al. 1998 clinical practice guidelines for the management of diabetes in Canada. *Can Med Assoc J* 1998;159(8 Suppl).
6. American Diabetes Association. Preconception care of women with diabetes. *Diabetes Care* 1998;21:S56-S59.
7. Ryan EA. Pregnancy in diabetes. *Med Clin North Am* 1998;82:823-45.
8. Lunt H. Women and diabetes. *Diabet Med* 1996;13:1009-16.
9. Tuomilehto J, Podar T, Tuomilehto-Wolf E, Virtala E. Evidence for importance of gender and birth cohort for risk of IDDM in offspring of IDDM parents. *Diabetologia* 1995;38:975-82.
10. Kitzmiller JL, Buchanan TA, Kjos S, Combs CA, Ratner RE. Pre-conception care of diabetes, congenital malformations, and spontaneous abortions. *Diabetes Care* 1996;19:514-41.
11. Leguizamón G, Reece EA. Effect of medical therapy on progressive nephropathy: influence of pregnancy, diabetes and hypertension. *J Maternal-Fetal Med* 2000;9:70-8.
12. Klein BEK, Moss SE, Klein R. Effect of pregnancy on progression of diabetic retinopathy. *Diabetes Care* 1990;13:34-40.
13. Chew EY, Mills JL, Metzger BE, Remaley NA, Jovanovic-Peterson L, Knopp RH, et al. Metabolic control and progression of retinopathy. *Diabetes Care* 1995;18:631-7.
14. Magee LA. Treating hypertension in women of child-bearing age and during pregnancy. *Drug Safety* 2001;24:457-74.
15. McElvy SS, Miodovnik M, Rosenn B, Khoury JC, Siddiqi T, St. John Dignan P, et al. A focused preconceptional and early pregnancy program in women with type 1 diabetes reduces perinatal mortality and malformation rates to general population levels. *J Maternal-Fetal Med* 2000;9:14-20.
16. Willhoite MB, Bennert HW, Palomaki GE, Zaremba MM, Herman WH, Williams JR, et al. The impact of preconception counseling on pregnancy outcomes. The experience of the Maine Diabetes in Pregnancy Program. *Diabetes Care* 1993;16:450-5.
17. Dunne FP, Brydon P, Smith T, Essex M, Nicholson H, Dunn J. Pre-conception diabetes care in insulin-dependent diabetes mellitus. *Q J Med* 1999;92:175-6.
18. Holing EV. Preconception care of women with diabetes: the unrevealed obstacles. *J Maternal-Fetal Med* 2000;9:10-3.
19. Holing EV, Shaw Beyer C, Brown ZA, Connell FA. Why don't women with diabetes plan their pregnancies? *Diabetes Care* 1998;21:889-95.
20. Janz NK, Herman WH, Becker MP, Charron-Prochownik D, Shayna VL, Lesnick TG, et al. Diabetes and pregnancy. Factors associated with seeking pre-conception care. *Diabetes Care* 1995;18:157-65.